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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,911	05/11/2007	Robert J. Aitken	NUSE-020/00US 307302-2068	7123

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EXAMINER	
KASTEN, ROBERT J	

ART UNIT	PAPER NUMBER
1795	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,911	AITKEN ET AL.	
	Examiner	Art Unit	
	ROBERT KASTEN	1795	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/15/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This is the first non-final action on the merits.

Claims 1-24 and 27 are pending in this application. Claims 1, 5-10, 12-14, 16-23 have been amended. No new matter has been added.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-24 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over ENGELMANN et al. (*Gamete Research* 19:151-159 (1988)), from here on referred to as ENGELMANN, in view of RYLATT et al. (WO 2004/101117), from here on referred to as RYLATT.

Concerning Claim 1, ENGELMANN teaches a method for the separation of a spermatozoa sample based on electrophoretic mobility (pg. 151, abstract). This necessarily teaches that a “sperm type” be separated from a “sperm population" in a “sperm sample.” The sample is separated by application of an electric potential (electric field, pg. 151, abstract). The separation yields a sperm type separated from another type (two classes of spermatozoa, pg. 151, abstract).

ENGELMANN does not expressly teach that the separation occurs through an ion-permeable membrane.

However, RYLATT teaches a process for separating a cell type from a cell mixture by electrophoresis (abstract), the electrophoretic separation being caused by application of an electric potential to a sample (pg. 2, lines 27-31) in the presence of and across an ion-permeable membrane (pg. 3, lines 1-11).

In the present case, the motivation for adding a membrane to the separation device of ENGELMANN would be to limit the convective mixing of separated samples in the device after separation had been performed (RYLATT, pg. 4, lines 24-29). The free-flow electrophoresis of ENGELMANN does not provide for a membrane, but rather a

flow system of substantially laminar flow perpendicular to a electric field (ENGELMANN, pg. 151, abstract). After separation of the spermatozoa, convective mixing of the separated sample (effectively undoing the separation already performed) would likely be limited due of the laminar flow profiles, but some mixing could certainly occur, leading to inefficient separation of sample. By using the ion-permeable membrane of RYLATT, convective mixing of the sample after separation has been shown to be substantially reduced, leading one of ordinary skill in the art to appreciate that separations performed on the sample would be unlikely to be undone by convective mixing of the sample during, for instance, a sample recovery step. Therefore, at the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to provide an ion-permeable membrane as in RYLATT in the device of ENGELMANN to eliminate convective mixing and facilitate more efficient separation of sample.

Concerning Claim 2, ENGELMANN teaches that the sperm types are separated according to electrophoretic mobility (pg. 153, lines 1-2), which led to separation based on the gender of the sperm cell (pg. 151, abstract).

Concerning Claim 3, ENGELMANN teaches that the separated sperm cells had nearly no change in viability, which means that fertilizing potential of the separated sperm cells will likely remain unchanged as well. Further, since the prior art method of ENGELMANN in view of RYLATT comprises the same steps as the prior art (see claim 2 rejection above) the prior art method is likely to have the same residual effects on the sperm cells, such as sperm cell fertilizing potential.

Concerning Claim 4, ENGELMANN does not expressly teach that the sperm type separated have an undesired characteristic such as those claimed.

However, RYLATT teaches that a method of electrophoretic separation of cells can either selectively remove wanted or unwanted cells from the sample (pg. 3, lines 24-28).

In the present case, the separation of a sperm cell from a sample based on either desired characteristics or undesired characterizes is a matter of design choice and intended use, as what could be considered undesired characteristics by one user could be desired characteristics by another user depending on the intended use of the separated sample. Further, the claimed "undesired characteristics" of claim 4 would necessarily be separable by the method of the prior art (ENGELMANN in view of RYLATT) because the prior art separation method is the same as the claimed method and is acting on the same material, leading one of ordinary skill in the art to expect success when separating the samples as claimed in this invention. Therefore, at the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to separate a sperm type based on the claimed characteristics as a matter of experimental/engineering design choice.

Concerning claim 5, ENGELMANN teaches that the electrophoretic separation of the spermatozoa takes place in a free-flow electrophoresis device (pg. 152, "Free-Flow Electrophoresis"). The method includes a step of applying an electric field perpendicular to a sample flow (pg. 152, "Free-Flow Electrophoresis").

ENGELMANN does not expressly teach the electrophoretic separation comprise the steps of providing an apparatus with multiple sample chambers and an ion-selective membrane.

However, RYLATT teaches a method for the electrophoretic separation of cells comprising the following steps:

- Providing a sample containing a mixture of cell types to a sample chamber of (an) electrophoresis apparatus comprising a first electrolyte chamber; a second electrolyte chamber, a first sample chamber disposed between the first electrolyte chamber and the second electrolyte chamber; a second sample chamber disposed adjacent to the first sample chamber disposed and between the first electrolyte chamber and the second electrolyte chamber; a first ion-permeable barrier disposed between the first sample chamber and the second sample chamber; a second ion-permeable barrier disposed between the first electrolyte chamber and the first sample chamber; a third ion-permeable barrier disposed between the second sample chamber and the second electrolyte chamber; and electrodes disposed in the first and second electrolyte chambers
- Applying an electric potential between the electrodes causing at least one cell type in the first sample chamber or the … second sample chamber to move through the first ion-permeable barrier into the other of the first or second sample chamber.

In the present case, one of ordinary skill in the art would have been motivated to include the ion-permeable barrier addition steps of RYLATT (and therefore necessarily include the sample chamber/buffer chamber addition steps from RYLATT as well) in the method of ENGELMANN to help substantially eliminate convective mixing of separated sample from the electrophoretic separation of sample (RYLATT, pg. 4, lines 24-29). The free-flow electrophoresis of ENGELMANN does not provide for addition of membranes, but rather a flow system of substantially laminar flow perpendicular to a electric field (ENGELMANN, pg. 151, abstract). After separation of the spermatozoa, convective mixing of the separated sample (effectively undoing the separation already performed) would likely be limited due of the laminar flow profiles, but some mixing could certainly occur, leading to inefficient separation of sample. By adding the ion-permeable membrane addition steps of RYLATT, convective mixing of the sample after separation has been shown to be substantially reduced, leading one of ordinary skill in the art to appreciate that separations performed on the sample would be unlikely to be undone by convective mixing of the sample during, for instance, a sample recovery step. Because RYLATT has shown the prior art method be capable of separating human cell types (pg. 3, lines 15-19), one of ordinary skill in the art would have also expected success when adding ion-permeable membrane addition steps to the method of ENGELMANN. Therefore, at the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to provide ion-permeable membrane addition steps as in RYLATT in the device of ENGELMANN to eliminate convective mixing and facilitate more efficient separation of sample.

Concerning Claim 6, ENGELMANN teaches that the sperm sample contain two populations of sperm (X and Y spermatozoa, pg. 151, title).

Concerning Claim 7, ENGELMANN teaches that separation of a spermatozoa sample could achieve nearly 100% purity of X spermatozoa (pg. 156, “Discussion”). In the present case, the choice of one purity of separated sample over another is a matter of engineering design choice. The claim language of "desired purity" necessarily requires that the purity of the resulting sample is chosen by the user of the invention, and not limited to a specific value. A nearly 100% pure sample as taught by ENGELMANN would be a desired purity to one of ordinary skill in the art for downstream methods requiring ultra-pure samples, such as for targeted/directed artificial insemination.

Concerning Claim 8, ENGELMANN in view of RYALTT teach all the limitations of claim 5. RYLATT further teaches that the pore size of a membrane is a known result effective variable and that the pore size (and therefore distribution) should be chosen based on the sizes of cells to be separated (RYLATT, pg. 4, lines 15-16).

Concerning Claim 9, ENGELMANN in view of RYALTT teach all the limitations of claim 5. Because of their use in electrophoresis, the prior art membranes are necessarily electrophoresis membranes. RYLATT further teaches that the pore size of any of the membranes is a known result effective variable (either the first membrane, RYLATT, pg. 4, lines 15-16, or the second and third, RYLATT, pg. 4, lines 19-21) and that the pore size (and therefore distribution) should be chosen based on the sizes of cells to be separated (RYLATT, pg. 4, lines 15-16) or other factors regarding the

separation (RYLATT, pg. 4, lines 19-21). Therefore, the membranes of the combination of ENGELMANN and RYLATT necessarily have a characteristic average pore size and distribution.

Concerning Claim 10, ENGELMANN in view of RYALTT teach all the limitations of claim 5. Further, RYLATT teaches that the first membrane be a large pore sized membrane (pg. 4, line 7).

Concerning Claim 11, ENGELMANN in view of RYALTT teach all the limitations of claim 10. Further, RYLATT teaches that the membrane can be a polycarbonate membrane (pg. 4, lines 7-8) with a pore size of 1 to 10 um (pg. 4, lines 13-14).

Concerning Claim 12, ENGELMANN in view of RYALTT teach all the limitations of claim 1. Further, ENGELMANN teaches an electric field strength of 80-120 V/cm (pg. 153, "Electrophoresis: Operating Conditions) and a flow chamber construed by the Examiner as being 120 mm long (pg. 152, "Free Flow Electrophoresis). Therefore, ENGELMANN teaches a separation voltage in the following range:

$$(80\text{-}120\ \text{V/cm}) \times .120\ \text{cm} = 9.6\text{-}14.4\ \text{V}$$

"Where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976)" (MPEP 2144.05 (I)).

Concerning Claim 13, ENGELMANN in view of RYALTT teach all the limitations of claim 1. Further, ENGELMANN teaches the applied current is to be selected by the user (pg. 153, “Electrophoresis: Operating Conditions").

ENGELMANN does not expressly teach a specific applied current in the prior art method.

However, RYLATT teaches that the electrophoresis voltages applied in the prior art method depend on the cell type, apparatus and medium used (pg. 5, lines 17-18).

In the present case, given that the current and voltage applied to the electrophoretic sample are known result effective variables (ENGELMANN, pg. 153, “Electrophoresis: Operating Conditions" and RYLATT, pg. 5, lines 17-18), the current applied to the device is necessarily taught by the prior art combination of ENGELMANN and RYLATT. The relationship of voltage to current is well known to those in the art, described by the equation :

$$V= iR$$

where V is the voltage, i is the current, and R is the resistance of the medium in which the electric potential will travel. Given that the methods of the prior art combination and the claimed invention in claim 1 are the same, the resistance of the medium is necessarily the same. Therefore, the current applied to the device will necessarily be taught in the prior art by virtue of the fact that the specific voltage is known to be an obvious choice and the resistance of the prior art is that of the claimed invention, these quantities being those that define the current applied to the device.

Concerning Claim 14, ENGELMANN in view of RYALTT teach all the limitations of claim 1. Further, ENGELMANN teaches an electric field strength of 80-120 V/cm (pg. 153, "Electrophoresis: Operating Conditions). "Where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976)" (MPEP 2144.05 (I)).

Concerning Claim 15, ENGELMANN does not expressly teach that the field strength applied in the prior art method if 16-20 V/cm.

However, RYLATT teaches that the electrophoresis field strengths applied in the prior art method depend on the cell type, apparatus and medium used (pg. 5, lines 17-18).

In the present case, the Examiner has determined that the field strength is a known result effective variable (RYLATT, pg. 5, lines 17-18). Because RYLATT teaches that the field strengths can vary not only based on cell type, but also on the apparatus and medium used, the teachings of ENGELMANN that the field strength being in a certain range do not necessarily teach away from the claimed field strengths. Therefore, one of ordinary skill in the art would have expected the method of ENGELMANN to be just as effective at the claimed electric field strength. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). The discovery of an optimum value of a known result effective variable, without producing any new or unexpected results, is within the ambit of a person of ordinary skill in the art. See *In re Boesch*, 205 USPQ 215

(CCPA 1980) (see MPEP § 2144.05, II.). Therefore, at the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to perform the method of ENGELMANN in view of RYLATT because optimizing the field strength applied in an electrophoretic method is a known result effective variable and therefore a matter of design choice.

Concerning Claim 16, ENGELMANN teaches that the electrophoresis is carried out for 80 seconds (pg. 153, "Electrophoresis: Operating Conditions).

ENGELMANN does not expressly teach the sample volume size.

In the present case, the sample volume is a matter of design choice. One of ordinary skill in the art would have chosen a sample volume based on the intended use of the sample. For instance, if large quantities of sperm cells were required in downstream experiments, then the sample volume applied in the prior art method would be larger. Smaller samples would have been separated if there was fear that a larger amount of sample separated would lead to a significant portion of that sample would go unused in downstream experiments and therefore wasted. Therefore, at the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to use the claimed sample volume in the prior art method of ENGELMANN in view of RYLATT as a matter of experimental design choice.

Concerning Claim 17, ENGELMANN teaches that electrophoresis buffer have a concentration of 10mM (pg. 152, "Buffer Systems").

Concerning Claims 18-19, ENGELMANN teaches that the sperm sample have a sperm density of 60-80 x 10^6 (cells)/mL (pg. 152, "Free-Flow Electrophoresis").

Concerning Claims 20-24, ENGELMANN teaches that the method produces a sperm sample which causes substantially no change is sperm cell viability (pg. 156, “Viability and Motility of Separated Spermatozoa”).

Concerning Claim 27, ENGELMANN in view of RYLATT teach a method of separating sperm cells with all the limitations of claim 1. Further, ENGELMANN teaches that separated sperm cells are useful in "planned parenthood (pg. 151, "Introduction")". From this teaching it would have been obvious to perform the claimed invention. In the present case, one of ordinary skill in the art would have known that the ENGELMANN teaching of separating sperm for use in planned parenthood would mean that the cells are separated into enriched samples in order to control and select genetic traits of a child between a human male and human female. Necessarily, the act of forming this child, thus making the owners of the sperm and ovum a “parent,” would require that these two cells make contact. The fertilization of an ovum by contact with a sperm is well known to those of skill in the art. Therefore, the teaching in ENGELMANN that the separated sperm can be used in planned parenthood necessarily teaches that the fertilization step as claimed be carried out after the method of claim 1.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT KASTEN whose telephone number is

(571)270-7598. The examiner can normally be reached on Mon-Thurs, 8am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen can be reached on 571-272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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